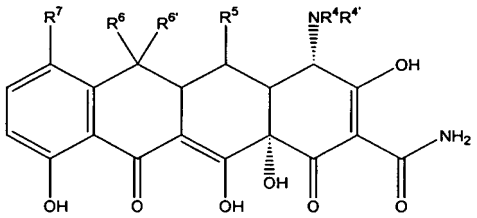
CLAIMS

1. A 7-substituted tetracycline compound which is substantially free of positional isomers, said compound having the formula:



(I)

wherein:

R^4 and $R^{4'}$ are each alkyl;

R^5 is hydrogen, hydroxyl, or a prodrug moiety;

R^6 and $R^{6'}$ are each independently hydrogen, hydroxyl, alkyl, or taken together, alkenyl;

R^7 is halo substituted, N-substituted or unsubstituted phenyl, and pharmaceutically acceptable salts thereof, wherein said tetracycline compound is substantially free of positional isomers.

2. The compound of claim 1, wherein R^5, R^6 and $R^{6'}$ are each hydrogen and R^4 and $R^{4'}$ are each methyl.

3. The compound of claim 1, wherein R^7 is unsubstituted phenyl.

4. The compound of claim 1, wherein R^7 is 2-substituted phenyl.

5. The compound of claim 4, wherein said compound is selected from the group consisting of 7-(2-fluorophenyl) sancycline, 7-(2-chlorophenyl) sancycline, 7-(2-bromophenyl) sancycline, and 7-(2-iodophenyl) sancycline.

6. The compound of claim 1, wherein R^7 is 3-substituted phenyl.

7. The compound of claim 6, wherein said compound is selected from the group consisting of 7-(3-fluorophenyl) sancycline, 7-(3-chlorophenyl) sancycline, 7-(3-bromophenyl) sancycline, and 7-(3-iodophenyl) sancycline.

8. The compound of claim 1, wherein R^7 is 4-substituted phenyl.

9. The compound of claim 8, wherein said compound is selected from the group consisting of 7-(4-fluorophenyl) sancycline, 7-(4-chlorophenyl) sancycline, 7-(4-bromophenyl) sancycline, 7-(4-iodophenyl) sancycline, 7-(4-trichloromethylphenyl) sancycline, 7-(4-trifluoromethylphenyl) sancycline, 7-(4-tribromomethylphenyl) sancycline, and 7-(4-triiodomethylphenyl) sancycline.

10. The compound of claim 1, wherein R^7 is 2-N-substituted phenyl.

11. The compound of claim 10, wherein said 2-N-substituted phenyl is substituted with a nitro group.

12. The compound of claim 11, wherein said compound is 7-(2-nitrophenyl) sancycline.

13. The compound of claim 10, wherein said 2-N-substituted phenyl is 2-amino substituted.

14. The compound of claim 13, wherein said 2-amino substituent is dialkylamino.

15. The compound of claim 14, wherein said dialkyl amino group is dimethylamino.

16. The compound of claim 13, wherein said compound is selected from the group consisting of 7-(2-aminophenyl) sancycline, 7-(2-N,N,-dimethylaminophenyl) sancycline, 7-(2-N,N,-diethylaminophenyl) sancycline, 7-(2-N,N,-dipropylaminophenyl) sancycline, and 7-(2-N,N,-dibutylaminophenyl) sancycline.

17. The compound of claim 1, wherein R^7 is 3-N-substituted phenyl.

18. The compound of claim 17, wherein said 3-N-substituted phenyl is substituted with a nitro group.

19. The compound of claim 18, wherein said compound is 7-(3-nitrophenyl) sancycline.

20. The compound of claim 17, wherein said 3-N-substituted phenyl is 3-amino substituted.

21. The compound of claim 20, wherein said 3-amino substituent is dialkylamino.

22. The compound of claim 21, wherein said dialkyl amino group is dimethylamino.

23. The compound of claim 20, wherein said compound is selected from the group consisting of 7-(3-aminophenyl) sancycline, 7-(3-N,N,-dimethylaminophenyl) sancycline, 7-(3-N,N,-diethylaminophenyl) sancycline, 7-(3-N,N,-dipropylaminophenyl) sancycline, and 7-(3-N,N,-dibutylaminophenyl) sancycline.

24. The compound of claim 1, wherein R^7 is 4-N-substituted phenyl.

25. The compound of claim 24, wherein said 4-N-substituted phenyl is substituted with a nitro group.

26. The compound of claim 25, wherein said compound is 7-(4-nitrophenyl) sancycline.

27. The compound of claim 24, wherein said 4-substituted phenyl is 4-amino substituted.

28. The compound of claim 27, wherein said 4-amino substituent is dialkyl.

29. The compound of claim 28, wherein said dialkyl amino group is dimethyl.

30. The compound of claim 29, wherein said compound is 7-(4-aminophenyl) sancycline, 7-(4-N,N,-dimethylaminophenyl) sancycline, 7-(4-N,N,-diethylaminophenyl) sancycline, 7-(4-N,N,-dipropylaminophenyl) sancycline, or 7-(4-N,N,-dibutylaminophenyl) sancycline.

31. A tetracycline compound which is substantially free of positional isomers, wherein said tetracycline compound is 7,9-diphenyl sancycline, and pharmaceutically acceptable salts thereof, wherein said tetracycline compound is substantially free of positional isomers.

32. The compound of any one of claims 1-31, wherein said compound is at least 75% free of positional isomers.

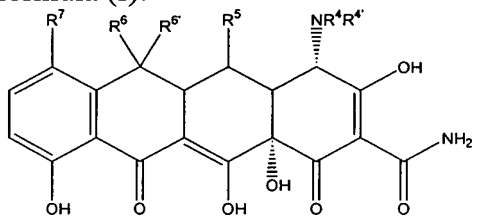
33. The compounds of claim 32, wherein said compound is at least 80% free of positional isomers.

34. The compounds of claim 33, wherein said compound is at least 85% free of positional isomers.

35. The compound of claim 34, wherein said compound is at least 90% free of positional isomers.

36. The compound of claim 35, wherein said compound is at least 95% free of positional isomers.

37. A method for treating a tetracycline responsive state in a mammal, comprising administering to said mammal a 7-substituted tetracycline compound, which is substantially free of positional isomers, of formula (I):



(I)

wherein:

R^4 and $R^{4'}$ are each alkyl;

R^5 is hydrogen, hydroxyl, or a prodrug moiety;

R^6 and $R^{6'}$ are each independently hydrogen, hydroxyl, alkyl, or taken together, alkenyl;

R^7 is halo substituted, N-substituted or unsubstituted phenyl; and pharmaceutically acceptable salts thereof, such that the tetracycline responsive state is treated, wherein said tetracycline compound is substantially free of positional isomers.

38. The method of claim 37, wherein R^5, R^6 and $R^{6'}$ are each hydrogen and R^4 and $R^{4'}$ are each methyl.

39. The method of claim 38, wherein R^7 is unsubstituted phenyl.

40. The method of claim 38, wherein R^7 is 2-substituted phenyl.

41. The method of claim 40, wherein said compound is selected from the group consisting of 7-(2-fluorophenyl) sancycline, 7-(2-chlorophenyl) sancycline, 7-(2-bromophenyl) sancycline, 7-(2-iodophenyl) sancycline, 7-(2-nitrophenyl) sancycline, 7-(2-aminophenyl) sancycline, 7-(2-N,N,-dimethylaminophenyl) sancycline, 7-(2-N,N,-diethylaminophenyl) sancycline, 7-(2-N,N,-dipropylaminophenyl) sancycline, and 7-(2-N,N,-dibutylaminophenyl) sancycline.

42. The method of claim 38, wherein R^7 is 3-substituted phenyl.

43. The method of claim 42, wherein said compound is selected from the group consisting of 7-(3-fluorophenyl) sancycline, 7-(3-chlorophenyl) sancycline, 7-(3-bromophenyl)

sancycline, 7-(3-iodophenyl) sancycline, 7-(3-nitrophenyl) sancycline, 7-(3-aminophenyl) sancycline, 7-(3-N,N,-dimethylaminophenyl) sancycline, 7-(3-N,N,-diethylaminophenyl) sancycline, 7-(3-N,N,-dipropylaminophenyl) sancycline, and 7-(3-N,N,-dibutylaminophenyl) sancycline.

44. The method of claim 38, wherein R^7 is 4-substituted phenyl.

45. The method of claim 44, wherein said compound is selected from the group consisting of 7-(4-fluorophenyl) sancycline, 7-(4-chlorophenyl) sancycline, 7-(4-bromophenyl) sancycline, 7-(4-iodophenyl) sancycline, 7-(4-trichloromethylphenyl) sancycline, 7-(4-trifluoromethylphenyl) sancycline, 7-(4-tribromomethylphenyl) sancycline, 7-(4-triiodomethylphenyl) sancycline, 7-(4-nitrophenyl) sancycline, 7-(4-aminophenyl) sancycline, 7-(4-N,N,-dimethylaminophenyl) sancycline, 7-(4-N,N,-diethylaminophenyl) sancycline, 7-(4-N,N,-dipropylaminophenyl) sancycline, and 7-(4-N,N,-dibutylaminophenyl) sancycline.

46. A method for treating a tetracycline responsive state in a mammal, comprising administering to said mammal 7,9-diphenyl sancycline and pharmaceutically acceptable salts thereof, which is substantially free of positional isomers, such that the tetracycline responsive state is treated, wherein said 7,9-diphenyl sancycline is substantially free of positional isomers.

47. The method of claim 37 or 46, wherein said tetracycline responsive state is a bacterial infection.

48. The method of claim 47, wherein said bacterial infection is associated with *E. coli.*

49. The method of claim 47, wherein said bacterial infection is associated with *S. aureus.*

50. The method of claim 47, wherein said bacterial infection is associated with *E. faecalis.*

51. The method of claim 47, wherein said bacterial infection is resistant to other tetracycline antibiotics.

52. The method of claim 37 or 46, wherein said compound is administered with a pharmaceutically acceptable carrier.

53. The method of any one of claims 37 or 46, wherein said compound is at least 75% free of positional isomers.

54. The method of claim 53, wherein said compound is at least 80% free of positional isomers.

55. The method of claim 54, wherein said compound is at least 85% free of positional isomers.

56. The method of claim 55, wherein said compound is at least 90% free of positional isomers.

57. The method of claim 56, wherein said compound is at least 95% free of positional isomers.

58. A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 1 or 31, and a pharmaceutically acceptable carrier.

59. The pharmaceutical composition of claim 58, wherein said compound is selected from the group consisting of 7-phenyl sancycline, 7, 9 diphenylsancycline, 7-(2-fluorophenyl) sancycline, 7-(2-chlorophenyl) sancycline, 7-(2-bromophenyl) sancycline, 7-(2-iodophenyl) sancycline, 7-(3-fluorophenyl) sancycline, 7-(3-chlorophenyl) sancycline, 7-(3-bromophenyl) sancycline, 7-(3-iodophenyl) sancycline, 7-(4-fluorophenyl) sancycline, 7-(4-chlorophenyl) sancycline, 7-(4-bromophenyl) sancycline, 7-(4-iodophenyl) sancycline, 7-(4-trichloromethylphenyl) sancycline, 7-(4- trifluoromethylphenyl) sancycline, 7-(4-tribromomethylphenyl) sancycline, 7-(4-triiodomethylphenyl) sancycline, 7-(2-nitrophenyl) sancycline, 7-(2-aminophenyl) sancycline, 7-(2-N,N,-dimethylaminophenyl) sancycline, 7-(2-N,N,-diethylaminophenyl) sancycline, 7-(2-N,N,-dipropylaminophenyl) sancycline, 7-(2-N,N,-dibutylaminophenyl) sancycline, 7-(3-nitrophenyl) sancycline, 7-(3-aminophenyl) sancycline, 7-(3-N,N,-dimethylaminophenyl) sancycline, 7-(3-N,N,-diethylaminophenyl) sancycline, 7-(3-N,N,-dipropylaminophenyl) sancycline, 7-(3-N,N,-dibutylaminophenyl) sancycline, 7-(4-nitrophenyl) sancycline, 7-(4-aminophenyl) sancycline, 7-(4-N,N,-dimethylaminophenyl) sancycline, 7-(4-N,N,-diethylaminophenyl) sancycline, 7-(4-N,N,-dipropylaminophenyl) sancycline, and 7-(4-N,N,-dibutylaminophenyl) sancycline.

60. The pharmaceutical composition of claim 58 or 59 wherein said compound is at least 75% free of positional isomers.

61. The pharmaceutical composition of claim 60, wherein said compound is at least 80% free of positional isomers.

62. The pharmaceutical composition of claim 61, wherein said compound is at least 85% free of positional isomers.

63. The pharmaceutical composition of claim 62, wherein said compound is at least 90% free of positional isomers.

64. The pharmaceutical composition of claim 63, wherein said compound is at least 95% free of positional isomers.